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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,741	10/10/2001	Om Reddy Gaddam	U 013662-3	8734
140	7590	06/17/2004	EXAMINER	
LADAS & PARRY 26 WEST 61ST STREET NEW YORK, NY 10023			RAO, DEEPAK R	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/975,741

Applicant(s)

GADDAM ET AL.

Examiner

Deepak R Rao

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,5-10,12-31 and 35-82 are pending in the application.
- 4a) Of the above claim(s) 3,5,6,12-26,35-77 and 79-82 are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7-10,27-31 and 78 are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 32904.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

Art Unit: 1624

### **DETAILED ACTION**

This office action is in response to the amendment filed on March 29, 2004.

Claims 1, 3, 5-10, 12-31 and 35-82 are pending in this application.

#### ***Election/Restrictions***

The elected invention of Group I, claims 1, 7-10, 27-31 and 78 are under consideration.

Claims 3, 5-6, 12-26, 35-77 and new claims 79-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

#### ***The following rejections are withdrawn and/or rendered moot:***

The rejection under 35 U.S.C. 112, first paragraph of the previous office action is rendered moot by cancellation of claims 11 and 32-34.

The rejections under 35 U.S.C. 112, second paragraph are either withdrawn in view of the amendments (e.g., in claim 1) or rendered moot by cancellation of claims (e.g., claims 11 and 32-34).

The rejection under 35 U.S.C. 102(b) of the previous office action is withdrawn in view of the amendments.

#### ***The following rejections are under new grounds:***

##### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1624

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-10 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the salt forms of the compounds and stereoisomers thereof, does not reasonably provide enablement for the derivatives, analogs, tautomeric forms or polymorphs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The specification fails to enable the preparation of the “derivatives”, “analogs”, “tautomeric forms”, and “polymorphs” of the claimed compounds. The specification provides examples showing the preparation of the claimed pharmaceutical salts of compounds of formula (I). However, there is no disclosure regarding the preparation of various ‘derivatives, analogs, polymorphs’, etc.

For example, the specification does not provide any explanation of what types of ‘derivatives’, ‘analogs’, ‘tautomeric forms’ are intended, how these are made, etc. The specification provides that ‘various polymorphs are prepared by crystallization of compound of formula (I) under different conditions’ (see page 13, lines 1-9), however, there are no working

Art Unit: 1624

examples of such polymorphs encompassed by the instant claims. The existence, structure and the properties (e.g., stability, solubility, bioavailability, rate of dissolution, etc.) of polymorphs tend to be very unpredictable. In order to establish the most stable polymorphic form, each has to be characterized and screened individually using various analytical techniques such as X-ray diffraction, thermal analysis, particle morphology characterization, etc.

In view of the lack of direction provided in the specification regarding the starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); *Ex parte Moersch*, 104 USPQ 122 (POBA 1954).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7-10 and 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claim 1 recites "A pharmaceutically acceptable salt of a compound of formula (I)", however, following this recitation a structural formula (III) is disclosed. Further, the structural formula (III) does not include any M, and the claim contains a definition for M.

Art Unit: 1624

2. The term “**derivative**” in the claims are confusing because it may be interpreted as a residue derived from the compounds of the claims. Also, it is not clear what “analogs” of the compounds are intended here. Further, it is not clear what ‘tautomeric forms’ of the compounds are intended by the instant claims. The specification does not provide any help.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 7-10, 27-31 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohray et al., WO 99/20614 in view of Claussner et al., U.S. Patent No. 5,646,172.

The primary reference, Lohray (WO'614) teaches a generic group of compounds which are structurally analogous to the compounds of formula (I) of the instant claims and the corresponding pharmaceutically acceptable salts. See the formula (I) in page 8 and the corresponding species, e.g., compound of Example 30. The reference further teaches the salts of the carboxylic acid moiety formed by organic bases such as lysine, guanidine, etc. see page 15, lines 25-32. The instant claims differ by reciting specific organic bases of the instant claims. The secondary reference, Claussner (US'172) in the analogous art of pharmaceutical compounds and the corresponding salts, discloses that salt forms of carboxylic acids formed by organic bases which organic bases include tris(hydroxymethyl) amino methane, dicyclohexylamine, N-methylglucamine, lysine, etc. (see col. 5, lines 17-23) and therefore, the secondary reference teaches the equivalence of the various organic bases. It would have been obvious to one of

Art Unit: 1624

ordinary skill in the art to prepare salts of the carboxylic acid compounds using any of the organic bases, including those taught by the secondary reference, as they are taught to be equivalent. One of ordinary skill in the art at the time of the invention would have been motivated to prepare the salts of the compounds of formula (I) disclosed in primary reference using any of the organic bases including those taught by the secondary reference. In view of the teachings of the secondary reference, the skilled chemist would have expected any of the organic bases to form salts having similar properties, because the secondary reference teaches that the organic bases are equivalent.

Receipt is acknowledged of the Information Disclosure Statement filed on March 29, 2004 and a copy is enclosed herewith.

### ***Conclusion***

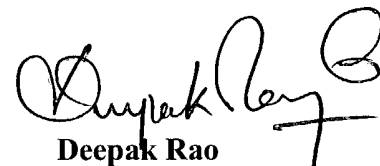
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Art Unit: 1624

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**Deepak Rao**  
**Primary Examiner**  
**Art Unit 1624**

June 10, 2004